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EXAMINER
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ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
09/28/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/579,769	STAEHLER ET AL.	
	Examiner	Art Unit	
	DAVID C. THOMAS	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 28, 2009 has been entered. Claims 1, 2, 9 and 10 (currently amended) and 3-8 and 11-33 (original or previously presented) will be examined on the merits.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Chetverin et al. (U.S. Patent No. 6,322,971).

Chetverin teaches a method for preparing at least one complementary copy of support-bound single-stranded nucleic acids (partial copies of parental strands are prepared on partialing arrays, and are in turn replicated to generate copies of the immobilized partial copy, column 24, lines 57-58 and Figure 5), comprising the steps:

(a) providing a support with a surface which comprises a plurality of positions at each of which different nucleic acid fragments are present, comprising base sequences which are complementary to the nucleic acids to be prepared (parental strands from the wells of a sorting array are transferred to the wells of a partialing array containing an immobilized primer, which is extended to produce a partial copy (part 33) of the parental strand (part 30), which is then removed to leave an immobilized single-stranded fragment, column 24, line 58 to column 25, line 21 and Figure 5A and Figure 5B, through the third step),

(b) adding nucleotide building blocks and an enzyme which brings about generation of different single-stranded nucleic acids from the complementary base sequences from (a) (the wells of the partialing array are then filled with a solution containing a universal primer, appropriate polymerase and the substrates and buffers needed to carry out copying the immobilized partial strands, column 25, lines 21-25),

(c) generating at least one single-stranded complementary copy of the nucleic acids to be prepared in (a) (after sealing the wells from each other, linear copying of the immobilized strands can be carried out simultaneously in all the wells of the array to produce copies 34 and 35, column 25, lines 25-28 and Figure 5B, last step), and

(d) detaching the nucleic acids generated in step (b) and, where appropriate, providing for further operations (further amplification of the immobilized partial strand can be achieved by PCR, which naturally releases single-stranded copies during the denaturation step, column 25, lines 35-44; amplified copies can then be transferred to a separate array to produce replicate arrays, column 4, lines 9-13 and 20-24 and column

10, line 66 to column 11, line 4; amplified DNA molecules produced on an array can be transferred, such as in a blotting procedure, from a partial array onto a mirror copy of the array, after melting the strands free from the other partial strand, column 73, lines 26-30; isolated strands from an array can also be inserted into vectors for cloning, or further amplified for sequencing, column 22, lines 26-29).

With regard to claim 2, Chetverin teaches a method for preparing a predetermined nucleic acid double strand (partial copies of parental strands are prepared on partialing arrays, and are in turn replicated to generate copies of the immobilized partial copy, column 24, lines 57-58 and Figure 5), comprising the steps:

(a) providing a support with a surface which comprises a plurality of positions at each of which different nucleic acid fragments are present, comprising base sequences which are chosen to be complementary to partial sequences of the nucleic acid double strand to be prepared (parental strands from the wells of a sorting array are transferred to the wells of a partialing array containing an immobilized primer, which is extended to produce a partial copy (part 33) of the parental strand (part 30), which is then removed to leave an immobilized single-stranded fragment, column 24, line 58 to column 25, line 21 and Figure 5A and Figure 5B, through the third step),

(b) adding nucleotide building blocks and an enzyme which brings about generation of complementary copies of the base sequences from (a) (the wells of the partialing array are then filled with a solution containing a universal primer, appropriate polymerase and the substrates and buffers needed to carry out copying the immobilized partial strands, column 25, lines 21-25),

(c) generating single-stranded complementary copies of the nucleic acids to be prepared in (a) (after sealing the wells from each other, linear copying of the immobilized strands can be carried out simultaneously in all the wells of the array to produce copies 34 and 35, column 25, lines 25-28 and Figure 5B, last step), and

(d) assembling the single-stranded partial sequences generated in step c) to give the desired nucleic acid double strand (double-stranded products are formed upon amplification of the immobilized partial strands by PCR, column 25, lines 35-44; alternatively, based on examination of overlapping terminal nucleotides of partial sequences, sequence blocks are first assembled and then ordered to determine the full sequence, column 6, lines 9-29, column 36, line 34 to column 37, line 44 and Figure 9A and 10A-C; sequences can also be covalently assembled together by ligation using an immobilized splint oligonucleotide, column 79, lines 54-60).

With regard to claims 3 and 4, Chetverin teaches a method characterized in that the support is selected from flat supports, porous supports, reaction supports with electrodes, reaction supports with particles or beads, microfluidic reaction supports which optionally have surface modifications such as gels, linkers, spacers, polymers, amorphous layers or/and 3D matrices, and combinations of the aforementioned supports (support is first prepared as a flat sheet or plain array, and then is converted by surface modifications into a sectional array by making physical depressions in a deformable solid support to isolate the areas in each depression to allow fluidic reactions to remain isolated from each other, column 4, lines 5-13, column 10, lines 14-26 and Figure 2 and 2A).

With regard to claim 5, Chetverin teaches a method characterized in that the nucleic acid fragments from (a) are generated by spatially resolved in situ synthesis on the support (reactions occurring in different wells of the array are highly specific based on the immobilized oligonucleotide in each well to allow a large number of separate amplification reactions to be performed in parallel, column 4, lines 13-16).

With regard to claims 6 and 7, Chetverin teaches a method characterized in that the nucleic acid fragments from (a) are synthesized by spatially or/and time-resolved illumination by means of a programmable light source matrix within the chambers of one or more reaction zones within a fluidic reaction chamber (immobilized fragments can be synthesized within the wells of a sectioned array by automated photolithography techniques such as light-directed spatially addressable parallel chemical synthesis, column 13, line 57 to column 14, line 3 and column 33, lines 26-30).

With regard to claim 8, Chetverin teaches a method characterized in that the assembly of the partial sequences in step (c) takes place at least partly in one or more steps on the support (sequences can be assembled together by ligation using an immobilized splint oligonucleotide as a template, column 79, lines 54-60).

With regard to claim 9, Chetverin teaches a method wherein the nucleic acid fragments from (a) are chosen so that the nucleic acids or partial sequences formed in step (c) can be joined to give nucleic acid double-stranded hybrids (oligonucletides immobilized to the support allow synthesis of a complete set of partial sequences of the nucleic acid of interest, which can then be ordered into a full sequence, column 6, lines 9-18).

With regard to claims 10 and 11, Chetverin teaches a method wherein a plurality of nucleic acids or partial sequences which form a strand of the nucleic acid double strand are covalently connected together comprising a treatment with ligase (sequences can be covalently assembled together by ligation using an immobilized splint oligonucleotide as a template, column 79, lines 54-60).

With regard to claim 12, Chetverin teaches a method characterized in that step (b) comprises the addition of at least one primer for each position of the support, the primer being complementary to part of the nucleic acid fragment located at this position and step (b) comprising an elongation of the primer (linear amplification of the hybridized strand is primed by the 3' end of the immobilized oligonucleotide and universal PCR primers are added, with extension of these primers resulting in PCR amplification of the sequence, column 16, lines 39-41 and 47-52 and Figure 4B, bottom).

With regard to claim 13, Chetverin teaches a method characterized in that double-stranded nucleic acid fragments are provided in step (a), with at least one strand being tethered to the surface of the support (masking oligonucleotides can be hybridized to the immobilized oligonucleotide prior to addition of the target strand, column 12, lines 19-26).

With regard to claim 14, Chetverin teaches a method characterized in that step (b) comprises transcription of double-stranded DNA fragments or/and replication of double-stranded RNA fragments (transcription reactions can be carried out in the wells

of a sectioned array if the immobilized oligonucleotide contains a promoter sequence, column 9, lines 56-60 and column 27, lines 55-60).

With regard to claims 15 and 17, Chetverin teaches a method characterized in that nucleic acid fragments or double-stranded, circular fragments comprising a self-priming 3' end are provided in step (a), and step (b) comprises elongation of the 3' end (some sequences of fragments formed on the array may contain perfect repeats that fold back on itself to serve as self-overlapping termini, which would naturally include the formation of circular type molecules, and thus can lead to extension using the same fragment as a template and thus compromise the ability to order sequence blocks, column 38, lines 26-41).

With regard to claims 16 and 18, Chetverin teaches a method which comprises elimination of the elongation product (formation of such ambiguities can be drastically reduced by using longer probes in such recursive sequence regions, and using larger amounts of all variable oligonucleotides on the array, column 38, line 58 to column 39, line 3).

With regard to claim 19, Chetverin teaches a method characterized in that the nucleic acid fragments from (a) are generated by:

- provision of capture probes at the positions (arrays comprise immobilized oligonucleotides complementary to the target sequences in order to bind the target strands at fixed locations in the array, column 3, lines 46-54 and column 8, lines 46-51) and

- binding of nucleic acid fragments from a fluid passed over the support to the capture probes (solutions are spread across the arrays containing the immobilized oligonucleotides, and include restriction digests of DNA samples added to the array after melting the strands, column 14, lines 53-54, column 16, lines 23-31 and Figure 5, first step), where the capture probes are complementary to partial regions of the nucleic acid fragments (the immobilized oligonucleotides are complementary to the variable and constant regions of the target strands, including internal sequences that allow partial products to be synthesized, column 5, lines 25-37, column 16, lines 32-38 and Figure 5, second step).

With regard to claims 20 and 32, Chetverin teaches a method wherein recognition sequences for specific interaction with molecules such as proteins, nucleic acids, peptides, drugs, saccharides, lipids, hormones or/and organic compounds are present at one or more positions in the sequence of the generated nucleic acids (the constant regions of the immobilized oligonucleotides can contain priming or transcription promoter sites that interact with primers through hybridization and polymerases that bind to the priming or promoter sites, column 9, lines 57-60 and column 27, lines 57-60).

With regard to claims 21 and 33, Chetverin teaches a method wherein the sequence of the generated nucleic acids is a naturally occurring sequence, a non-naturally occurring sequence or a combination thereof (the immobilized oligonucleotides are synthetic nucleic acids made directly on the support or attached to the support after synthesis, and contain sequences complementary to natural sequences present in the sample nucleic acids, column 12, line 41 to column 13, line 3, column 13, lines 4-31 and

column 16, lines 31-36; the nucleic fragments can comprise a strand from a melted restriction fragment obtained from a DNA sample, column 16, lines 22-36).

With regard to claim 22, Chetverin teaches a method characterized in that the sequence is taken from a database, from a sequencing experiment or from an apparatus for integrated synthesis and analysis of polymers (arrays can be synthesized by an automated process, column 13, lines 32-47, and can comprise constant region sequences common to all probes and variable region sequences that are complementary to different sequences of the target, column 9, lines 20-33 and Figure 1A).

With regard to claim 23, Chetverin teaches a method characterized in that the nucleotide building blocks may comprise naturally occurring nucleotides, modified nucleotides or mixtures thereof (immobilized oligonucleotides bound to nucleic acid templates are extended using an appropriate DNA polymerase and nucleotides, column 29, lines 32-34; extension can also be performed by only one nucleotide using dideoxynucleotides as substrates for the DNA polymerase, column 29, lines 34-39).

With regard to claims 24 and 25, Chetverin teaches a method characterized in that modified nucleotide building blocks are used for labeling and subsequent detection of the nucleic acids or of the joined nucleic acid double strands in a light-dependent or/and electrochemical manner (the dideoxynucleotides used in extension reactions can be tagged with different labels such as fluorescent dyes to provide for detection by scanning the arrays at different wavelengths, column 29, lines 41-49).

With regard to claims 26 and 27, Chetverin teaches a method wherein said prepared nucleic acids are tools for therapeutic, pharmacological or diagnostic purposes (the method is useful for surveys of selected oligonucleotides for clinical diagnostic procedures, column 7, lines 12-16; RNA copies can be produced from RNA polymerase promoter sequences introduced in primer sequences, which could be used for anitsense or miRNA applications, column 69, lines 22-27).

With regard to claim 28, Chetverin teaches a method further comprising transferring said prepared nucleic acids into effector cells (isolated sequences from an array can be inserted into vectors for cloning and transformation of microbial cells, column 22, lines 26-29 and column 2, lines 54-57).

With regard to claims 29 and 30, Chetverin teaches a method wherein said prepared nucleic acids are stabilized, condensed or/and topologically manipulated during a stepwise combination and joining or subsequent thereto, wherein the stabilization, condensation or/and topological manipulation is effected by functional molecules such as histones or topoisomerases (isolated sequences from an array can also be inserted into vectors for cloning, which upon transformation into microbial cells, will undergo natural condensation and topological manipulations *in vivo*, column 22, lines 26-29 and column 2, lines 54-57).

With regard to claim 31, Chetverin teaches a method wherein said prepared nucleic acids are propagatable cloning vectors (isolated sequences from an array can also be inserted into vectors for cloning, column 22, lines 26-29; transcription sites can

be placed adjacent to target sequences using primers containing promoters for amplification, column 9, lines 57-60).

Response to Arguments

4. Applicant's arguments filed July 28, 2009 have been fully considered but they are not persuasive.

Applicant argues that the 35 USC § 102 rejection of claims 1-33 over Chetverin et al. (U.S. Patent No. 6,322,971) should be withdrawn since the cited reference fails to disclose all the limitations of the claims as amended. In particular, with regard to independent claims 1 and 2, Applicant argues that the method of Chetverin relates to making copies of oligonucleotide sequences found in a sample by extension of support-bound primers that hybridize to the sample sequences to thus produce copies of target sequences that also contain the support-bound sequence. Applicant argues that this in contrast to the presently claimed method that relates to making a copy of the support-bound template sequence by adding an enzyme and nucleotide building blocks to form a single-stranded complementary copy of the bound template. Applicant further argues that Chetverin does not teach nucleic acid fragments bound to the support which are chosen to be complementary to the nucleic acids to be prepared, but rather teaches that primer sequences on the support hybridize to the target sequences and are extended upon addition of a polymerase and nucleotide building blocks and thus does not teach generation of single-stranded complementary copies of the sequences chosen to be complementary to the nucleic acids to be prepared. The Examiner asserts that while

Chetverin teaches extension of support-bound primers (such as on a sorting array, Figure 4B), the reference also teaches replication of support-bound single-stranded nucleic acid strands, such as those shown in the second to last step of Figure 5B (a partialing array). Thus, a support is provided containing a plurality of positions of different nucleic acid fragments, and these fragments are complementary to copies produced by the next step, replication of the immobilized strand (bottom of Figure 5B). The immobilized sequence in this case was "chosen" by the previous step of adding parental sequence strands to the partialing array to form the immobilized sequence, but the chosen sequence is also complementary to the replicated copies that are available for further use.

With regard to claim 2, Applicant further argues that Chetverin does not teach making a complementary copy of the nucleic acids on the support which are chosen to be complementary to the nucleic acids to be prepared, but rather teaches extension of support-bound primers that hybridize to a region within the target to produce complimentary copies of the sample nucleic acid that contains the primer sequence, rather than generating sequences complementary to support-bound nucleic acid fragments. The Examiner asserts that Chetverin teaches both extension of primers bound to an array to produce complementary copies of target nucleic acids, but also expressly teaches the limitations of claim 2, since the immobilized strands that represent partial copies of a parental strand (Figure 5B, second to last step) also serve as the starting point of claim 2, that is, "a surface comprising a plurality of positions at each of which different nucleic acid fragments are present, comprising base sequences

which are chosen to be complementary to the nucleic acids to be prepared". Chetverin further teaches that such sequences can be copied in a linear fashion to produce single-stranded products or by PCR to produce double-stranded products (column 25, lines 25-28 and 35-44), either of which can be used in downstream processes such as assembling partial sequences by ligation using splint oligonucleotides (column 79, lines 54-60). Therefore, for all the reasons stated above, the 102(b) rejection of claims 1-33 over Chetverin is maintained.

Summary

5. Claims 1-33 are rejected. No claims are allowable.

Correspondence

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320 and whose fax number is 571-273-3320. The examiner can normally be reached on 5 days, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David C Thomas/
Examiner, Art Unit 1637

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637